OH R^6 R^3 CH-CH-NH-C-A R^5 (IV) R^2 $NHSO_2R^1$

LUS CONTRACTOR TO THE CONTRACT

wherein

R¹ is lower alkyl, aryl or arylakyl;

R² is hydrogen, hydroxy, alkoxy, -CH₂OH, cyano, -C(O)OR⁷, -CO₂H, -CONH₂, tetrazole, -CH₂NH₂ or halogen;

R³ is hydrogen, alkyl, heterocycle or

R^{8"} R^{8'}

R⁴ is hydrogen, alkyl or B;

 $R^5, R^{5'}, R^8, R^{8'} \text{ and } R^{8''} \text{ are independently hydrogen, alkoxy, lower alkyl, halogen,} \\ -OH, -CN, -(CH_2)_nNR^6COR^7, -CON(R^6)R^{6'}, -CON(R^6)OR^{6'}, -CO_2R^6, -SR^7, -SOR^7, -SO_2R^7, \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^{6'}, -NR^6COR^7, -OCH_2CON(R^6)R^{6'}, -OCH_2CO_2R^7 \text{ or aryl; or } \\ -N(R^6)SO_2R^1, -N(R^6)R^6, -N(R^6)R^6$

R⁵ and R⁵ or R⁸ and R⁸ may together with the carbon atoms to which they are attached form an aryl or heterocycle;

R⁶ and R⁶ are independently hydrogen or lower alkyl; and R⁷ is lower alkyl;

R⁹ and R⁹ are independently hydrogen, lower alkyl, alkyl, cycloalkyl, arylalkyl, aryl, heteroaryl; or

R⁹ and R⁹ may together with the nitrogen atom to which they are attached form a heterocycle;

A is abond, $-(CH_2)_n$ - or -CH(B)-, wherein n is an integer of 1, 2 or 3 and B is -CN, $-CON(R^9)R^{9}$ - or $-CO_2R^7$;

with the proviso that when A is a bond or $-(CH_2)_n$ - and R^3 is hydrogen or unsubstituted alkyl, then R^4 is B or substituted alkyl;

(b) the compound of formula (V) is represented by the following general formula:

OH H R^2 CHCH₂N -C $(X)_m$ R^4 N N R^6 R^6 R^6 (V)
wherein

n is 0 to 5;

m is 0 or 1;

r is 0 to 3;

A is pyridinyl;

R¹ is (1) hydroxy, (2) oxo, (3) halogen, (4) cyano, (5) NR⁸R⁸, (6) SR⁸, (7) trifluoromethyl, (8) C₁-C₁₀ alkyl, (9) OR⁸, (10) SO₂R⁹, (11) OCOR⁹, (12) NR⁸COR⁹, (13) COR⁹, (14) NR⁸SO₂R⁹, (15) NR⁸CO₂R⁸, or (16) C₁-C10 alkyl substituted by hydroxy,

Soll To

A' cont-

.halogen, cyano, NR⁸R⁸, SR⁸, trifluoromethyl, OR⁸, C₃-C₈ cycloalkyl, phenyl, NR⁸COR⁹, COR⁹, SO₂R⁹, OCOR⁹, NR⁸SO₂R⁹ or NR⁸CO₂R⁸;

R and R³ are independently (1) hydrogen, (2) C_1 - C_{10} alkyl or (3) C_1 - C_{10} alkyl with 1 to 4 substituents selected from hydroxy, C_1 - C_{10} alkoxy, or halogen;

X is (1)
$${}^{-}$$
CH₂-, (2) -CH₂-, (3) -CH=CH- or (4) -CH₂O-;

 R^4 and R^5 are independently (1) hydrogen, (2) C_1 - C_{10} alkyl, (3) halogen, (4) NHR⁸, (5) OR⁸, (6) SO₂R⁹ or (7) NHSO₂R⁹;

 R^6 is (1) hydrogen or (2) C_1 - C_{10} alkyl;

 R^7 is $Z-(R^{1a})_n$;

R^{1a} is (1) R¹, (2) C₃-C₈ cycloalkyl, (3) phenyl optionally substituted with up to 4 groups independently selected from R⁸, NR⁸R⁸, OR⁸, SR⁸ or halogen, or (4) 5 or 6-membered heterocycle with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, optionally substituted with up to four groups independently selected from oxo, R⁸, NR⁸R⁸, OR⁸, SR⁸, or halogen;

Z is (1) phenyl, (2) naphthyl, (3) or a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (4) a benzene ring fused to a C₃-C₈ cycloalkyl ring, (5) a benzene ring fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, (6) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen fused to a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms selected from oxygen, sulfur or nitrogen, or (7) a 5 or 6-membered heterocyclic ring with from 1 to 4 heteroatoms

 R^8 is (1) hydrogen, (2) C_1 - C_{10} alkyl, (3) C_3 - C_8 cycloalkyl, (4) Z optionally having 1 to 4 substituents selected from halogen, nitro, oxo, $NR^{10}R^{10}$, C_1 - C_{10} alkyl, C_1 - C_{10} alkoxy, C_1 - C_{10}

Sub Carl

the curt.

Lalkylthio, and C_1 - C_{10} alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO_2 H, CO_2 - C_1 - C_{10} alkyl, SO_2 - C_1 - C_{10} alkyl, C_3 - C_8 cycloalkyl, C_1 - C_{10} alkoxy, or Z optionally substituted by from 1 to 3 halogen, C_1 - C_{10} alkyl or C_1 - C_{10} alkoxy, or (5) C_1 - C_{10} alkyl having 1 to 4 substituents selected from hydroxy, halogen, CO_2 H, CO_2 - C_1 - C_{10} alkyl, SO_2 - C_1 - C_{10} alkyl, C_3 - C_8 cycloalkyl, C_1 - C_{10} alkoxy, C_1 - C_{10} alkyl, or Z optionally substituted by from 1 to 4 halogen, C_1 - C_{10} alkyl or C_1 - C_{10} alkoxy;

 R^9 is (1) R^8 or (2) NR^8R^8 ; and

 R^{10} is (1) C_1 - C_{10} alkyl, or (2) two R^{10} groups together with the N to which they are attached forming a 5 or 6-membered ring optionally substituted with C_1 - C_{10} alkyl;

(c) the compound of formula (VI) is:

$$X$$
 $CH-CH_2-NH$
 OR
wherein

X is hydrogen, halogen, trifluoromethyl or lower alkyl, and

R is hydrogen; lower alkyl which may have a suitable substituent selected from the group consisting of $\operatorname{cyclo}(C_3-C_7)$ alkyl, hydroxy, lower alkoxy, carboxy and lower alkoxycarbonyl; $\operatorname{cyclo}(C_3-C_7)$ alkyl or lower alkanoyl;

(d) the compound of formula (VII) is represented by the following general formula:

 R^{2} R^{1} $CHOH-CH_{2}-NH-C(R^{6})R^{7}-Y-X$ $O-Z-CO_{2}H$ (VII)

Ri wherein

R¹ is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl, hydroxymethyl, methyl, methoxyl, amino, formamido, acetamido, methylsulphonylamido, nitro, benzyloxy, methylsulphonylmethyl, ureido, trifluoromethyl or p-methoxybenzylamino group;

R² is a hydrogen, fluorine, chlorine or bromine atom or a hydroxyl group;

R³ is a hydrogen, chlorine or bromine atom or a hydroxyl group,

R⁴ is a hydrogen atom or a methyl group,

R⁵ is a hydrogen atom or a methyl group;

R⁶ is a hydrogen, fluorine or chlorine atom or a methyl, methoxyl or hydroxy group;

X is an oxygen atom or a bond;

Y is an alkylene group of up to 6 carbon atoms or a bond; and

Z is an alkylene, alkenylene or alkynylene group of up to 10 carbon atoms; and

(e) the compound of formula (VIII) is represented by the following general formula:

$$R^{1}$$
 R^{2}
 R^{6}
 R^{7}
 R^{8}
 R^{8}
 R^{8}
 R^{8}
 R^{8}

wherein

R is hydrogen or methyl,

R¹ is hydrogen, halogen, hydroxy, benzyloxy, amino or hydroxymethyl,

R²\is hydrogen, hydroxymethyl, -NHR³, -SO₂NR⁴R^{4'} or nitro,

R³ is hydrogen, methyl, -SO₂R⁵, formyl or -CONHR⁶',

R⁴ and R⁴ are independently hydrogen, lower alkyl or benzyl,

R⁵ is lower alkyl, benzyl or -NR⁴R⁴,

R⁶ is hydrogen or lower alkyl,

R6' is hydrogen or lower alkyl,

R⁹ is hydrogen, amino, acetylamino or hydroxy, and

X is N, O, S or methylene,

provided that when X is N, Oor S,

then R⁹ is hydrogen, either R⁷ or R⁸ is hydrogen, and the other is hydrogen, amino, acetylamino or hydroxy; and

provided that when X is methylene,

then both R⁷ and R⁸ are hydrogen.

11. (New) The method of Claim 10 that comprises administering a β_3 adreneric receptor agonist of formula (IV) or a salt thereof.

12. (New) The method of Claim 10 comprising administering the compound of formula (V) or a salt thereof.

13. (New) The method of Claim 10, comprising administering a β_3 adreneric receptor shown by the following formula (VI) or a salt thereof.

14. (New) The method of Claim 10, comprising administering a β_3 adreneric receptor agonist shown by the following formula (VII) or a salt, ester or amide thereof.

Jus Cont

cont.

Cub Cost

15. (New) The method of claim 10, comprising administering a β_3 adreneric receptor agonist shown by the following formula (VIII) or a salt thereof.

16. (New) The method of claim 10 wherein said compound is in the form of a prodrug.

17. (New) A method for the prophylactic and/or the therapeutic treatment of pollakiuria or urinary incontinence comprising administering to a subject in need thereof an effective amount of the β_3 adrenergic receptor agonist of claim 10 or a pharmaceutically acceptable salt thereof.

18. (New) A method for the prophylactic and/or the therapeutic treatment of nervous pollakiuria, neurogenic bladder dysfunction, nocturia, unstable bladder, cystospasm, chronic cystitis, chronic prostatitis, overflow incontinence, passive incontinence, reflex incontinence, urge incontinence, urinary stress incontinence comprising administering to a subject in need thereof an effective amount of the β_3 adrenergic receptor agonist of claim 10 or a pharmaceutically acceptable salt thereof.

19. (New) A commercial package comprising: the compound of claim 10 and written matter associated therewith,

wherein the written matter states that the pharmaceutical composition can or should be used for preventing and/or treating dysuria.

20. (New) An article of manufacture comprising: a packaging material and the compound of claim 10,